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The use of radiobiological TCP and NTCP models to validate the dose calculation algorithm and readjust the prescribed dose

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Purpose: This study introduces an advanced method to evaluate and extent the adjustment of the prescribed dose to maintain the same clinical results, when changing the dose calculation algorithm type (a), i.e density correction method to more recently type (b) algorithm, i.e AAA.
Material and methods: 10 cases with lung cancer were studied. For each case, 3 treatment plans were generated. Plan 1 was generated using type (a) algorithm, and Plan 2 using type (b) algorithm. In plan 3 the dose was calculated with type (b) algorithm using monitor units from plan 1 as input. A global analysis based on 2D and 3D gamma (γ) was made to evaluate the under / overestimation of calculated dose. Clinical evaluation was carried out using Tumour Control Probability (TCP) and Normal Tissue Complication Probabilities (NTCP) based on Uniform Equivalent Dose model. Assuming a constant TCP, the ratio "R= TCP/NTCP" and Uncomplicated Tumor Control Probability (UTCP) were calculated to measure the clinical benefit – toxicity. Wilcoxon test was used to evaluate the significance of the differences and the correlation coefficient (r) was calculated using Spearman's rank test.
Results: The dose calculated with algorithm type (b) was significantly overestimated to organs at risks while the delivered dose in MU was underestimated, $p < 0.001$. Therefore, γ maps confirmed the dosimetric results. Moreover, there were a significant difference for NTCP for lung and heart. The ratio "R" from plan 1 and plan 2 were significantly different, indicating that to maintain the same effect benefit and toxicity the prescribed dose should be readjusted.
Conclusion: We assessed the prescribed dose using the radiobiological models. The ratio of benefit was significantly changed when moving from type (a) algorithm to type (b) algorithm. This indicate that the prescribed dose should be readjusted when type (b) algorithm will be integrated in radiation oncology. A discussion between oncologist and physicist is quite necessary in order to readjust the prescribed dose.

Key words: TCP, NTCP, EUD, gamma maps.

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62 MeV Proton beams induced DNA damage in hypoxic conditions.

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Purpose: Hypoxia represents one of the most important challenges of current radiotherapy that can potentially affect the treatment planning and outcome. For the optimization of proton therapy and its application in treating hypoxic tumors such as dose and LET painting it is important to study the DNA damage response of normal cells under hypoxic and radio resistant conditions. The present study is aimed at understanding the variations in DNA double strand breaks induction and repair along prisitine and Spread-Out-Bragg-Peak Proton beams under hypoxic.
Materials and methods: DNA DSB damage and repair response was studied in AG01522 cells irradiated at various positions along the 62 MeV therapeutic protons Bragg peak at the CATANA beam line of the Institute of Nuclear Physics (INFN) Catania, Italy. Hypoxia was mimicked by using Cobalt chloride (CoCl2) and Dimethyl Sulphoxide (DMSO) was used as a Reactive Oxygen Species (ROS) scavenger. Hypoxia induction was confirmed by immunofluorescent staining of Hypoxia inducible factor-1 alpha (HIF-1α) and DNA DSB induction was quantified using p53 Binding protein-1 (53BP1) foci.
Results: The presence of DMSO and CoCl2 reduced the 53BP1 foci by 40% as compared to foci induction under normoxic conditions (30 minutes) in the cells irradiated at the entrance position of pristine beam. Cells irradiated at the Bragg peak revealed a significant induction of residual DSB damage even in presence of DMSO and CoCl2 at 24 hrs. Cells irradiated at distal end positions of the SOBP also revealed a significant induction of the 53BP1 foci irrespective of the oxygenation conditions of the medium.
Conclusions: Our results indicate the variations in the induction and repair of DNA DSBs in presence of ROS scavenger and Hypoxia along the Bragg peak. These findings can be of potential application in the tumor treatment planning of hypoxic tumors especially near the critical organs and combining DNA repair inhibitors approach.

Key words: Hypoxia, 53BP1, SOBP

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Laser accelerated ultra high dose rate protons induced DNA damage under hypoxic conditions

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Purpose: Hypoxic tumors still pose a challenge for modern radiotherapy. Hadrontherapy has gained momentum world wide as an effective modality for tumor therapy including success in inducing cell death in cancer cells under hypoxia as reported by several investigators. Significant advances in laser technologies have led to the prospect of using laser-accelerated ions, emitted in ultrashort bursts, as a future, cost-saving alternative to conventional accelerators. An understanding of the radiobiological effects at the ultrahigh dose rate delivered by these short ions pulses on human cells under hypoxic conditions is important for the development and further advancement of this technology towards clinical applications.
Materials and methods: Laser accelerated 15-18 MeV protons generated using the Nd:glass VULCAN laser system at the Rutherford Appleton Laboratory, Oxford, UK, were delivered, by a compact magnetic transport system, to cell samples at dose rates exceeding 10^9 Gy/s. Dosimetry was validated using EBT2 gafchromic films and CR-39 tracks detector. Normal human skin fibroblasts (AG01522 cells) monolayers grown in custom made stainless steel, on 3 μm thin Mylar dishes were pre-gassed with hypoxic gas mixture (95% nitrogen and 5% Carbon-di-oxide) for 4 hours and irradiated inside portable beam-line hypoxia chambers. Hypoxia induction was confirmed using HIF-1 alpha immuostaining. DNA damage and repair kinetics was studied using 53BP1 foci formation assay up to 24 hours after irradiation under both normoxic and hypoxic conditions.
Results: Our preliminary data suggests the effectiveness of Laser accelerated protons in DNA damage induction under both normoxic and hypoxic conditions. We observed a small reduction in average foci induction at initial time points in hypoxic cells, which was not seen after 2 hrs.

Conclusions: We report here for the first time measurements of DNA damage with pulsed protons at ultrahigh dose rate (10^9-10^{10} Gy/s) under hypoxic conditions.

Key words: 53BP1, HIF-1 alpha,

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Faster QA through improved proton calorimetry. Another spin-off from particle physics

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We have used the calorimeter module originally designed for the SuperNEMO experiment to measure the energies of protons at the Clatterbridge proton therapy cyclotron.
Such measurements are necessary for time consuming QA checks, and by improving the rates and energy resolution this time can be considerably reduced.
Preliminary results show that an energy resolution of sigma 0.7% can be achieved for low rates which will later be compared to the high rate data. We hope to extend this technique to proton radiography as well.

Keywords: proton therapy, radiography, scintillator

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Study of Dosimetric Characteristics of a commercial OSLD system

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Introduction: Cancer treatment by radiotherapy is a complex process and needs accurate radiation treatment delivery and can be verified using in vivo measurements. Optically stimulated luminescence dosimeter [OSLD] has been used extensively for beam dosimetry, radiation protection including in vivo measurements due to their simple readout process and multiple times readout facility.
Aim and Objective: The aim of the present work is to study the dosimetric characteristics of commercial OSL system by Landauer Inc. before using it for clinical practice in radiotherapy.
Material and Methods: The OSLD system used is a commercial InLight™ microstar reader system, manufactured by Landauer Inc. The detector consist of Al_2O_3:C nanodot as OSL material, enveloped in special light protective plastic holders. In the present study the irradiations are carried out in 30*30 cm^2 solid water slab phantoms. Bhabhatron – II cobalt 60 telecobalt radiation is used for most of the measurements carried out. Clinac – iX is also used for 6 MV and 10MV energy photon beams to study dose rate and energy dependence. Absolute dose is measured using a 30013 PTW ionization chamber in solid water and compared with OSL dosimeter measurements.
Unless otherwise mentioned, all irradiations carried out using an SSD setup (80cm for co-60 and 100cm for linac) with 10*10cm^2 field size.OSL response with given dose is investigated for doses ranging from 0.5 to 4Gy. Energy dependence of OSL is investigated for Co-60, 6MV, 10MV beams, delivering a dose of 50 cGy each. Further the dose rate dependence of OSL detector is evaluated for dose rates of 200, 400, 600 cGy/min in accelerator with 6MV energy beam. We also studied the field size dependence by irradiating OSLD chips to 50 cGy dose for various field sizes ranging from 4*4 to 35*35 cm^2 for cobalt -60 beam. The dosimeter angular response is studied at various gantry angles from 90º to 270º, at an interval of 30º, with and without build up respectively.
Results: In present study it was observed that the OSL dose deviation is about - 4.5% as compared with ionization chamber. Further the reproducibility of detector is found to be within 3.44% standard deviation, with COV 0.035. There is no significant energy dependence of Al_2O_3:C detector for the energy range Co-60 to 10MV. The detector response was found to be linear in the dose range of 0.5 to 4Gy. The detector response is almost independent in clinical dose rate range, nearly independent of field size and is independent to angle of incidence of beam.
Discussion: The dosimetric characteristics of OSL system were studied and found that OSL response is energy and dose rate independent. The stability of system and linear dose response relationship makes it a good dosimeter for in vivo dosimetry in clinical radiotherapy.

Keywords: OSLD, invivo dosimetry, radiotherapy

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Simulation of recombination in an air filled ionization chamber

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Background: Air filled ionization chambers are the dosimeters of choice for photon therapy as well as particle therapy. Dosimetry protocols for ion beams take recombination effects into account, where the generated charge in the ionization chamber may recombine before it is picked up by the electrode. It is well established that intra-track recombination (initial recombination) is negligible in medical photon and electron beams, but must be accounted for in beams with heavy ions. However, the underlying assumptions for establishing the recommended method for correction for inter-track recombination (general recombination) still remains unclear today [1]. The current two-voltage method only is applicable for low LET-beams, with no initial recombination present [2,3], and this progress report focuses on a detailed recombination study of ion beams.
Here, we calculate the columnar recombination when the ion track is

- parallel to the electric field
- rotated with an angle between 0 and $\pi/2$ relative to the external field which was estimated analytically by Jaffé [4] and later confirmed experimentally by Kanai et al [5].

The general recombination is investigated by

- sampling two parallel ion tracks at different separation and initialized at different times
- comparing the simulation of a continuous beam with Greening's formula [6] for collection efficiency.

Simulations are confirmed by comparison with experimental data.
Methods: We have investigated positive and negative charge carrier distributions (CCDs) by solving the differential equation using a finite difference approach,

$$\frac{\partial n_{\pm}}{\partial t} = -D_{\pm}\nabla^2 n_{\pm} \mp \vec{\nabla}\cdot\left(\mu_{\pm}\vec{E}n_{\pm}\right) - \alpha n_{+}n_{-}$$

with derived from the initial CCDs, the diffusion constant, the mobility, for positive and negative CCDs, $\vec{E}$ the electric field vector, and the recombination constant.
Results: Our simulations reproduced the analytical solution from Jaffé and the experimental results by Kanai et al. On this platform we could also verify the Greening analytical solution.
Conclusion: The simulations of pulsed and continuous beams are seen to agree well with the known theories and experimental data, and the program is thus capable of reproducing the initial and general recombination processes taking place in high LET-beams. This allows a deeper study of the actual recombination processes taking place when several ion tracks are present and ultimately account for the overall recombination in air filled ionization chambers irradiated with high LET-beams.

Keywords: ionization chambers, recombination, high LET